First, applicant appreciates the Examiner's review of the art cited by applicant. Since the last office action, applicant filed another supplemental information disclosure statement. Applicant requests that the Examiner review the art cited there as well.

Turning to the action on the merits, applicant notes that claims 1-36, presumably claims 37-72, were rejected under 35 U.S.C. §112, second paragraph. In certain instances, it was difficult to determine the claims rejected by the Examiner since the office action listed claims no longer pending. Additionally, applicant disagrees with the rejections made. Nevertheless, in an effort to advance prosecution or at least to greatly reduce the number of issues on appeal, applicant has canceled the claims, or at least the terms, that were believed to be rejected. Accordingly, applicant believes this rejection has been obviated.

Therefore, applicant believes that claims 37, 45-54, 58-60, 71 and 72 comply with the requirements of 35 U.S.C. §112, second paragraph. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. §112 be withdrawn.

Claims 37-72 were also rejected under 35 U.S.C. §103(a) as being unpatentable over Press Release 09/30/99: Bristol-Myers Squibb Files New Drug Application for Novel Oral Antidiabetic Drug (hereafter "PR") in view of Erle et al. Acta Diabetol (1999) 36:61-65 (hereafter "Erle et al."). Applicant respectfully traverses this rejection.

According to the rejection, PR discloses a method of using metformin and glyburide as initial therapy for patients with type 2 diabetes. Erle et al. disclose that it is known to use low-dose glyburide plus metformin. Therefore, it would be obvious to use the low dose glyburide of Erle et al. in the method of PR.

Erle et al. clearly refers *only* to a low dose of glyburide. (Note that the lowest dose of metformin given in Erle et al. is 800 mg.) Even still, the very *lowest* dose of glyburide given in Erle et al. is 5 mg. PR does not suggest any dosing at all.

It is argued in the rejection that dosing is not recited in the broadest claim. While applicant does not believe it should be necessary to do so in view of the art used in the rejection, applicant is making every effort to advance the prosecution of this application. Consequently, once this amendment is entered, all the pending claims will include dosages. Nowhere is the kind of dosing claimed contemplated in Erle et al. or PR. Moreover, this kind of dosing is not suggested by the combination of Erle et al. and PR. Therefore, the combination of Erle et al. and PR does not make obvious applicant's invention.

For these reasons, applicant requests that this rejection be withdrawn.

In view of the foregoing, reconsideration of this application, entry of this amendment, withdrawal of the rejections, consideration of the supplemental information disclosure statement filed since the last office action, and allowance of all the pending claims are all respectfully requested.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

--37. A method for first line treatment of type 2 diabetes, in a drug naive human patient, which comprises administering to a drug naive human patient in need of treatment, as first line therapy, a low dose of a combination of metformin and glyburide, wherein the metformin in said low dose combination is administered in a daily dosage in an amount within the range from about 160 mg to about 750 mg, and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg. --

--54. The method as defined in Claim 53 wherein the 250 mg metformin/1.25 mg glyburide dosage is administered to a patient with a baseline hemoglobin A_{1c} (HbA_{1c}) > 9% or a fasting glucose > 200 mg/dL twice daily, with dosage increases[, where necessary,] in increments of 250 mg metformin/1.25 mg glyburide every 2 weeks, up to the minimum effective daily dose necessary to achieve adequate glycemic control. --

--71. A method for lowering blood glucose in a hyperglycemic human patient, which comprises administering to a drug naive human patient in need of treatment, as first line therapy, a therapeutically effective amount of a low dose of a combination of metformin and glyburide, wherein the metformin in said low dose combination is administered in a daily dosage in an amount within the range from about 160 mg to about 750 mg, and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg.

72. A method for decreasing insulin resistance, decreasing hemoglobinA_{1c}, increasing post-prandial insulin levels or decreasing post-prandial glucose excursion, individually or in any combination, in a human patient, which comprises administering to a drug naive human patient in need of treatment as first line therapy, a therapeutically effective amount of a low dose of a combination of metformin and glyburide, wherein the metformin in said low dose combination is administered in a daily dosage in an amount within the range from about 160 mg to about 750 mg, and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg.--